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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
PAK, JOHN D	
ART UNIT	PAPER NUMBER
1616	20

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/173,531	Applicant(s) Ellison et al.
	Examiner John Pak	Art Unit 1616

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Nov 25, 2002*

2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1, 2, 4-12, 14-17, and 21-29* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideratio

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1, 2, 4-8, 10-12, 14-17, and 21-29* is/are rejected.

7) ☒ Claim(s) *4-12 and 24-29* is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examine

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *19*
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

Claims 1-2, 4-12, 14-17 and 21-29 are pending in this application.

Applicant is advised that claims 10-12 and **23**-29 depend on the canceled claim 3. Correction is needed.

Claim 23 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 23 is solely dependent on the canceled claim 3. Claim 23 therefore cannot be further interpreted or examined.

Claims 10-12, 24-29 are objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend from a canceled claim (claim 3). See MPEP § 608.01(n).

Applicant is advised that "such treatment" in claim 1, line 2, would be improved by deleting that phrase and inserting --- said treatment --- .

Claims 4-9 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claims 4-8 ultimately depend on claim 1, but they do not correspond to the newly amended version of claim 1 wherein the solid tumors have been limited to those of the breast, colon, ovary, kidney, CNS, bladder, prostate and lung.

Applicant is advised that claim 9 is included in this objection because of its dependency to claim 4, but if it were presented in independent form, including all of the limitations of claim 1, it may be deemed allowable in the next Office Action, *pending* a search update at that time.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-2, 4-8, 10-12, 14-17, 21-22 and 24-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combined teachings of CN 1121807, CN 1079391, Li et al., Stephens et al. and Shimotsuura et al. in view of Shen et al., Konig et al. and JP 51-88620 for the reasons fully stated in Paper No. 13.

Applicant's remarks relative hereto have been given due consideration but they were deemed unpersuasive. Applicant argues that none of the cited documents discloses treating solid tumors of the breast, colon, ovary, kidney, CNS, bladder, prostate or lung, by administering to a human patient a therapeutically effective amount of one or more arsenic compounds or prodrug thereof.

The Examiner cannot agree. CN 1121807 teaches treating liver cancer, as well as leukemia and lymphatic cancer, with a solution formulated with 1-10 g arsenic trioxide, 8 g sodium chloride and 1000 ml water. 10 ml injection per day is disclosed for adults, with

different dosage and concentrations being possible based on age and condition (translation p. 5, last full paragraph). CN 1079391 teaches treating cervical cancer, as well as skin cancer and other "in vivo cancer entities" (translation page 8, lines 3-5) with arsenic compounds. Suspended injection and liposome are used (paragraph bridging translation pages 7-8). Shimotsuura et al. further establish the antineoplastic action of arsenic trioxide. Konig et al. teach that the organic arsenic compound melarsoprol has similar antineoplastic activity as arsenic trioxide and induces apoptosis. JP 51-88620 teaches that a mixture of ferrous, arsenic and sulfate ions can "cure cancerous disease of stomach, duodenum, uterus, lung, pancreas, etc." (see applicant's provided abstract). Remaining references further teach various arsenic compounds for treating leukemia.

Clearly, arsenic as an active agent has been amply disclosed by the prior art as having widely applicable antineoplastic activity. Solid tumors such as tumors of the liver, cervix, skin, "in vivo cancer entities," stomach, duodenum, uterus, lung and pancreas have all been taught to be treated with compositions that contain arsenic as an active agent. Given such divergent uses and activity, in light of recent clinical success in treating APL with arsenic trioxide (e.g. Shen et al.), one having ordinary skill in the art would have been motivated to utilize arsenic compounds as claimed, including on those tumors recited in claims 4-8, with the expectation that a treatment (e.g. alleviation, containment or reduction of symptoms or tumors) would be obtained.

Claim 2 requires that the solid tumor being treated is metastatic, but chemotherapeutic antineoplastic agents are known to be used on metastatic solid tumors. One having ordinary skill in the art would have been motivated to utilize the advantageous antineoplastic properties of

arsenic compounds on localized tumors as well as metastatic tumors since both types of tumors must be treated and reduced for the patient to remain alive.

Implantation device is noted as a dependent claim feature (claim 17), but the Examiner's position has been that arsenic has been taught to be delivered via many different carrier systems, including liposomes (CN 1079391). Liposomes are interpretable as implantation device.

Intravenous dosage amount of 0.5-150 mg/day is noted as a dependent claim feature (claims 21-22), CN 1121807 establishes operative concentration and dose amounts: 1-10 g arsenic trioxide per 1000 ml, wherein 10 ml is injected per day for adults, with different dosage and concentrations being possible based on age and conditions. Such dosage amounts overlap with the claimed dosage amount range.

Prodrug feature in the claims is noted, but the prior art establishes that it is the arsenic that has antineoplastic activity. Delivery of arsenic would have been expected to deliver antineoplastic activity, and therefore, one having ordinary skill in the art would have been motivated to utilize arsenic in many variety of forms, including a form in which it may be considered a "prodrug."

Arsenic in other forms and compound types are noted as dependent claim features (claims 24-26), but again, it is the arsenic that the ordinary skilled artisan would have used to deliver antineoplastic activity, and selection of arsenic halide, sulfide and organic form (e.g. malarsoprol) would have been suggested from their ready availability and ability to deliver the arsenic source to the cancer patient.

Oral (e.g., pill/tablet) forms of administration are typical in administering pharmacological agents, and one having ordinary skill in the art would have been motivated to utilize any one of the many modes of administration that are available, such as orally with pill or tablet, to deliver the active arsenic containing antineoplastic composition.

Therefore, the claimed invention, as a whole, would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, because every element of the invention and the claimed invention as a whole have been fairly suggested by the teachings of the cited references.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Most of the references listed on the PTO-1449 of 11/25/02 have been crossed out. The crossed-out references were either already considered and of record, or a copy has not been provided.

A facsimile center has been established in Technology Center 1600. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier numbers for accessing the facsimile machines are (703) 308-4556 or (703) 305-3592.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Examiner Pak whose telephone number is (703) 308-4538. The Examiner can normally be reached on Monday through Friday from 7:30 AM to 4 PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's Supervisor, Mr. José Dees, can be reached on (703) 308-4628.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-1235.

JOHN PAK
PRIMARY EXAMINER
GROUP 1600